

PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	Inferred duration of infectious period of SARS-CoV-2: rapid scoping review and analysis of available evidence for asymptomatic and symptomatic COVID-19 cases
AUTHORS	Byrne, Andrew; McEvoy, David; Collins, Aine; Hunt, Kevin; Casey, Miriam; Barber, Ann; Butler, Francis; Griffin, John; Lane, Elizabeth; McAloon, Conor; O'Brien, Kirsty; Wall, Patrick; Walsh, Kieran; More, Simon

VERSION 1 – REVIEW

REVIEWER	Billy Quilty London School of Hygiene and Tropical Medicine, United Kingdom
REVIEW RETURNED	13-May-2020

GENERAL COMMENTS	An excellent, thoughtful contribution. My only comments are that the x-axis of Figure 1, 2 and 4 should be labelled clearly. Well done.
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REVIEWER	Sen Pei Columbia University, United States
REVIEW RETURNED	15-May-2020

GENERAL COMMENTS	<p>In this manuscript, authors presented a comprehensive review of recent studies on the duration of infectious period of SARS-CoV-2. Results from virological studies, tracing studies and modelling studies for both asymptomatic and symptomatic infections were synthesized and compared. A large variation in the reported infectious period was observed, and estimates from modelling studies are typically shorter than those obtained from virological and tracing studies. The paper is well organized and the tables are helpful for researchers to track the recent findings on the viral dynamics and infectiousness of SARS-CoV-2. Here I have a few questions and suggestions.</p> <p>1. Virological and tracing studies are mostly based on small numbers of samples (shown in Tables 1-3), which are typically biased to patients with more severe symptoms or within outbreak clusters (thus easier to track). The estimates of infectious period for those infections may be relatively longer than the average value for general population. This can partially explain the longer estimates in these studies.</p> <p>2. The infectious period of SARS-CoV-2 depends on many factors such as viral dynamics, symptoms (cough and sneeze), protective measures (social distancing, wearing face masks), treatment (hospitalized, isolated), etc. As a result, in modeling works, it is a</p>
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	<p>context-dependent concept. For instance, in a country with better protective measures and aggressive interventions, the infectious period should be shorter in the model due to control efforts. So, in different types of studies, the interpretation of “infectious period” should be different: for virological and tracing studies, it is the natural time period during which transmission is possible upon effective contact without intervention; however, in modeling studies, it factors in the effect of control measures (isolation or quarantine). Such nuanced difference should be discussed.</p> <p>3. In line 42, “Some current models may be underestimating infectious period”. I suggest removing this statement as the actual infectious period in general population, especially those undetected cases, is unknown.</p> <p>4. In line 293, why use maximum latent period minus the serial interval?</p> <p>5. Fig. S1 is important and should be moved to the main text, with some explanations.</p> <p>6. Some contents in “Overall duration findings” overlap with the contents in the Results section. Would it be possible to summarize findings in itemized bulletins?</p> <p>7. Figure 5 could be modified to the same style of other figures.</p>
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VERSION 1 – AUTHOR RESPONSE

Reviewer: 1

Reviewer Name: Billy Quilty

Institution and Country: London School of Hygiene and Tropical Medicine, United Kingdom

Please state any competing interests or state ‘None declared’: None declared

Please leave your comments for the authors below

An excellent, thoughtful contribution. My only comments are that the x-axis of Figure 1, 2 and 4 should be labelled clearly. Well done.

- We would like to extend our gratitude for reviewing our paper
- We have edited the figures as suggested and made the -axis more clear for readers

Reviewer: 2

Reviewer Name: Sen Pei

Institution and Country: Columbia University, United States

Please state any competing interests or state ‘None declared’: None declared

Please leave your comments for the authors below

In this manuscript, authors presented a comprehensive review of recent studies on the duration of infectious period of SARS-CoV-2. Results from virological studies, tracing studies and modelling studies for both asymptomatic and symptomatic infections were synthesized and compared. A large variation in the reported infectious period was observed, and estimates from modelling studies are typically shorter than those obtained from virological and tracing studies. The paper is well organized and the tables are helpful for researchers to track the recent findings on the viral dynamics and infectiousness of SARS-CoV-2. Here I have a few questions and suggestions.

1. Virological and tracing studies are mostly based on small numbers of samples (shown in Tables 1-

3), which are typically biased to patients with more severe symptoms or within outbreak clusters (thus easier to track). The estimates of infectious period for those infections may be relatively longer than the average value for general population. This can partially explain the longer estimates in these studies.

- We concur with the reviewer. This is a good point, and could help to explain some of the variation between the observed inferred infectious duration estimates and the outcomes from some modelling papers

- We have added in the following to the discussion: “It should be noted that some of the virological and tracing studies reviewed had small sample sizes (see Study Limitations) and potentially biased towards more severe cases or clusters of infection. It is unknown as to whether these cases are representative of infectious periods generally across populations. However, if symptom severity is linked to infectious duration, one could speculate that this bias could help to explain the some of the difference between model and empirical duration estimates.”

2. The infectious period of SARS-CoV-2 depends on many factors such as viral dynamics, symptoms (cough and sneeze), protective measures (social distancing, wearing face masks), treatment (hospitalized, isolated), etc. As a result, in modeling works, it is a context-dependent concept. For instance, in a country with better protective measures and aggressive interventions, the infectious period should be shorter in the model due to control efforts. So, in different types of studies, the interpretation of “infectious period” should be different: for virological and tracing studies, it is the natural time period during which transmission is possible upon effective contact without intervention; however, in modeling studies, it factors in the effect of control measures (isolation or quarantine). Such nuanced difference should be discussed.

- This is another good point, and hints to another conclusion, that language is important. If different disciplines are speaking with different meanings for the same word, we will be in trouble. We have tried to avoid this problem, as much as possible, with our clear conceptual model in figure S1. We are trying to get estimates for infectious period, in the absence of truncation. So, for example, one of the modelling paper describes an infectious period that is truncated once a patient is diagnosed and isolated (in hospital), in which case the parameter would for generally be considered an ‘infectious period’.

- We have added the following to the discussion: “An important factor to consider when comparing parameter estimates between empirical and modelling studies is the interpretation of the parameter by different disciplines, and even between researchers from the same discipline. The infectious period can be considered significantly context specific and dynamic, and the ability to transmit infection can be modulated by interventions (e.g. through isolation or hospitalisation). Modelling papers, depending on the model structure, can report truncated infectious period accounting for such interventions. Such estimates are not comparable with our definition of the parameters reviewed, and we have attempted to avoid such disparities where we found them.”

3. In line 42, “Some current models may be underestimating infectious period”. I suggest removing this statement as the actual infectious period in general population, especially those undetected cases, is unknown.

- We accept that the premise is debatable, and have removed the statement.

4. In line 293, why use maximum latent period minus the serial interval?

- This was what the authors presented in their paper, and there may be some questions around this approach to estimating infectious period.

5. Fig. S1 is important and should be moved to the main text, with some explanations.

- We are limited by the number of recommended figures presented in BMJ Open papers, therefore we have kept this figure in the supplementary material.

6. Some contents in “Overall duration findings” overlap with the contents in the Results section. Would it be possible to summarize findings in itemized bulletins?

- While we understand the benefit of brevity, we feel the discussion reads better as a narrative piece instead of bulletpoints. However, in cognisance of the reviewers point, we have tried to edit down some of the content.

7. Figure 5 could be modified to the same style of other figures.

- We have recreated these using gamma distributions in stata.

Thank you.

VERSION 2 – REVIEW

REVIEWER	Sen Pei Columbia University
REVIEW RETURNED	05-Jun-2020
GENERAL COMMENTS	All my questions are properly addressed.